AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph on page 8, line 19 to page 11, line 5, as follows:

As a cyclic compound, WO02/62795 discloses dihydropyrazolo[3,4-b]pyridine derivatives [ethyl 4-(6-chloro-2, 2, 4-trimethyl-3,4-dihydro-2H-1,4-benzoxazin-8-yl)-6-propyl-2,4-dihydro-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, etc.: glycogen synthase kinase-3 beta (GSK-3β) inhibitor]; WO02/22074 and WO01/12607 disclose 3-aryl-4-quinolone derivatives [7-methoxy-3-(4-methoxyphenyl)-1-methyl-5-phenylquinolin-4(1H)-one, 8-methoxy-3-(4-methoxyphenyl)-1-methyl-5-phenylquinolin-4(1H)-one, etc.: prevention for post-angioplasty intraluminal restenosis, proliferation of clonogenic cells in malignant tumours]; WO99/62520 discloses 3,4-dihydro-2H-1,4-benzoxazine derivatives [4-(8-benzyl-4-methyl-3,4-dihydro-2H-1,4-benzoxazin-6-yl)-2,4-dioxobutanoic acid, etc.: treatment for HIV infection]; Bulletin des SCB (1997), 106(7-8), 467-474 discloses quinazoline derivatives [ethyl 1,7-dimethyl-4-oxo-3,5-diphenyl-1,2,3,4-tetrahydroquinazoline-6-carboxylate: synthesis]; Zhongguo Yaowu Huaxue Zazhi (1995), 5(3), 187-191 discloses 4-quinolone-3-carboxylic acid derivatives [1-cyclobutyl-6,8-difluoro-7-(4-~~methylpiperadin~~methylpiperazin-1-yl)-4-oxo-5-phenoxy-1,4-dihydroquinoline-3-carboxylic acid: antibacterial agent]; J. Med. Chem., (1993), 36(19), 2801-9 discloses 4-quinolone-3-carboxylic acid derivatives [1-cyclopropyl-7-(2,6-dimethylpyridin-4-yl)-6,8-difluoro-4-oxo-5-(phenylthio)-1,4-dihydroquinoline-3-carboxylic acid: topoisomerase II inhibitor]; EP0343574 discloses 4-quinolone derivatives [1-ethyl-8-methoxy-5-phenylquinolin-4(1H)-one, etc.: a cardiac]; JP-A S63-258855 discloses 4-quinolone-3-carboxylic acid derivatives [1-cyclopropyl-6,8-difluoro-7-(4-~~methylpiperadin~~methylpiperazin-1-yl)-4-oxo-5-(phenylthio)-1,4-dihydroquinoline-3-carboxylic acid: animal drug]; EP272914 discloses benzoxazinylpyridazinone derivatives [4,6-dimethyl-8-(4-methyl-6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)-2H-1,4-benzoxazin-3(4H)-one, 4,6-dimethyl-8-(6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)-2H-1,4-benzoxazin-

3(4H)-one, 2,2,4-trimethyl-8-(6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)-2H-1,4-benzoxazin-3(4H)-one, etc.: a cardiac]; J. Med. Chem., (1972), 15(3), 237-241 discloses 4-quinolone-3-carboxylic acid derivatives [8-chloro-1-methyl-4-oxo-5-phenyl-1,4-dihydroquinoline-3-carboxylic acid: dehydrogenase inhibitor]; DE10021568 discloses pyrimidinyl phthalazinyl sulfoxide derivatives [8-[(4,6-dimethoxypyrimidin-2-yl)sulfinyl]-4-methyl-2-phenylphthalazin-1(2H)-one, etc.: agricultural chemical]; Acta. Chemica. Sloveniva (2000), 47(2), 187-203 discloses pyrazolo[3,4-d]pyrimidine derivatives [3-[(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)amino]-6-methyl-1,7-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one: synthesis]; WO03/39131 discloses pyrazolo[4,3-d]pyrimidine derivatives [6-(4-bromophenyl)-1-(4-methoxyphenyl)-5-methyl-7-oxo-6,7-dihydro-1H-pyrazolo[4,3-d]pyrimidine-3-carbonitrile: Factor Xa inhibition]; JP-A H11-501923 discloses pyrazolo[3,4-d]pyrimidine derivatives [3,6-dibenzyl-1-cyclopentyl-1,7-dihydro-4H-pyrazolo[3,4-d]pyrimidin-4-one: c-GMP phosphodiesterase inhibition]; Bulletin de la Soc. Chim. de France (1995), 132(7), 67580 discloses pyrazolo[3,4-d]pyrimidine derivatives [methyl (6-tert-butoxy-4-oxo-1,3-diphenyl-1,4-dihydro-5H-pyrazolo[3,4-d]pyrimidin-5-yl)acetate: synthesis]; and WO98/54116 discloses pyrrolo[2,3-d]pyrimidine derivatives [1,3,6-trimethyl-5-phenyl-1H-pyrrolo[2,3-d]pyrimidine-2,4(3H,7H)-dione: cancer].

Please amend the paragraph on page 19, line 17 to page 20, line 5 as follows:

(15) The compound according to the above-mentioned (1), wherein the compound is 3-(~~2,4-Dimethylphenyl~~2,4-dimethylphenyl)-6-dipropylamino-1,5-dimethyl-1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one,

5-(~~2,4-Dimethylphenyl~~2,4-dimethylphenyl)-3-methyl-1-(1-propylbutyl)quinolin-4(1H)-one,

1-(~~Dipropylamino~~dipropylamino)-6-mesityl-3-methyl-4H-quinolizin-4-one,

2-(~~Dipropylamino~~dipropylamino)-5-mesityl-3,7-dimethyl-3,7-dihydro-*4H*-pyrrolo[2,3-*d*]pyrimidin-4-one,

1-(~~2,4-Dimethylphenyl~~2,4-dimethylphenyl)-4-(1-ethylpropoxy)-6-methyl-1,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyridazin-7-one,

5-~~Mesityl~~mesityl-3-methyl-1-(1-propylbutyl)cinnolin-4(*1H*)-one, or

1-(1-ethylpropyl)-4-mesityl-2-methyl-1,2-dihydro-*3H*-indazol-3-one,

Please amend the paragraph on page 34, line 22 to page 35, line 19 as follows:

Examples of the "substituted hydroxy" for R^1 include a hydroxy which is substituted with an optionally substituted hydrocarbyl (e.g., C_{1-15} alkyl, C_{1-15} alkenyl, C_{1-15} alkynyl, C_{1-15} cyclic hydrocarbon, each of which may be substituted with an optionally halogenated alkyl, amino, alkoxy, carbamoyl, aryl, heterocyclic group, hydroxy, etc. at a suitable position; preferably, C_{1-8} alkyl group such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, neopentyl, tert-pentyl, hexyl, isohexyl, heptyl, octyl, etc., which may be substituted at a suitable position with halogen, nitro, cyano, alkoxy, amino, substituted amino, or the like, a C_{3-10} alkenyl group, a C_{3-10} alkynyl group, a C_{3-7} cycloalkyl group, a C_{3-7} alkylcycloalkyl group, a C_{5-7} cycloalkenyl group, a C_{5-7} alkylcycloalkenyl group, an aromatic group (e.g., phenyl group, pyridyl group, etc.), benzyl group, or an alkylaromatic group (e.g. ~~benzyl group,~~ methylpyridyl group, etc.)); an optionally substituted heterocyclic group (e.g., a 5- to 10-membered saturated or unsaturated heterocyclic group including bicyclic ring such as piperidine, pyrrolidine, etc.) or an optionally substituted acyl (e.g., acyl formed by combining carbonyl with the above-mentioned optionally substituted hydrocarbyl).

Please amend the paragraph on page 35, line 20 to page 36, line 15 as follows:

Examples of the "substituted sulfanyl" for R^1 include a sulfanyl which is substituted with an optionally substituted hydrocarbyl (e.g., C_{1-15} alkyl, C_{1-15} alkenyl, C_{1-15} alkynyl, C_{1-15} cyclic hydrocarbon, each of which may be substituted with an optionally halogenated alkyl, amino, alkoxy, carbamoyl, aryl, heterocyclic group, hydroxy, etc. at a suitable position;

preferably, C_{1-8} alkyl group such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, neopentyl, tert-pentyl, hexyl, isohexyl, heptyl, octyl, etc., which may be substituted at a suitable position with halogen, nitro, cyano, alkoxy, amino, substituted amino, or the like, a C_{3-10} alkenyl group, a C_{3-10} alkynyl group, a C_{3-7} cycloalkyl group, a C_{3-7} alkylcycloalkyl group, a C_{5-7} cycloalkenyl group, a C_{5-7} alkylcycloalkenyl group, an aromatic group (e.g., phenyl group, pyridyl group, etc.), benzyl group, or an alkylaromatic group (e.g. ~~benzyl group,~~ methylpyridyl group, etc.)); or an optionally substituted heterocyclic group (e.g., a 5- to 10-membered saturated or unsaturated heterocyclic group including bicyclic ring such as piperidine, pyrrolidine, etc.).

Please amend the paragraph on page 36, line 16 to page 37, line 11, as follows:

Examples of the "optionally substituted sulfinyl" for R^1 include a sulfinyl which may be substituted with an optionally substituted hydrocarbyl (e.g., C_{1-15} alkyl, C_{1-15} alkenyl, C_{1-15} alkynyl, C_{1-15} cyclic hydrocarbon, each of which may be substituted with an optionally halogenated alkyl, amino, alkoxy, carbamoyl, aryl, heterocyclic group, hydroxy, etc. at a suitable position; preferably, C_{1-8} alkyl group such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, neopentyl, tert-pentyl, hexyl, isohexyl, heptyl, octyl, etc., which may be substituted at a suitable position with halogen, nitro, cyano, alkoxy, amino, substituted amino, or the like, a C_{3-10} alkenyl group, a C_{3-10} alkynyl group, a C_{3-7} cycloalkyl group, a C_{3-7} alkylcycloalkyl group, a C_{5-7} cycloalkenyl group, a C_{5-7} alkylcycloalkenyl group, an aromatic group (e.g., phenyl group, pyridyl group, etc.), benzyl group, or an alkylaromatic group (e.g. ~~benzyl group,~~ methylpyridyl group, etc.)); or an optionally substituted heterocyclic group (e.g., a 5- to 10-membered saturated or unsaturated heterocyclic group including bicyclic ring such as piperidine, pyrrolidine, etc.).

Please amend the paragraph on page 37, line 12 to page 38, line 7 as follows:

Examples of the "optionally substituted sulfonyl" for R^1 include a sulfonyl which may be substituted with an optionally substituted hydrocarbyl (e.g., C_{1-15} alkyl, C_{1-15} alkenyl, C_{1-15} alkynyl, C_{1-15} cyclic hydrocarbon, each of which may be substituted with an optionally halogenated alkyl, amino, alkoxy, carbamoyl, aryl, heterocyclic group, hydroxy, etc. at a suitable position; preferably, C_{1-8} alkyl group such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, neopentyl, tert-pentyl, hexyl, isohexyl, heptyl, octyl, etc., which may be substituted at a suitable position with halogen, nitro, cyano, alkoxy, amino, substituted amino, or the like, a C_{3-10} alkenyl group, a C_{3-10} alkynyl group, a C_{3-7} cycloalkyl group, a C_{3-7} alkylcycloalkyl group, a C_{5-7} cycloalkenyl group, a C_{5-7} alkylcycloalkenyl group, an aromatic group (e.g., phenyl group, pyridyl group, etc.), benzyl group, or an alkylaromatic group (e.g. ~~benzyl group,~~ methylpyridyl group, etc.)); or an optionally substituted heterocyclic group (e.g., a 5- to 10-membered saturated or unsaturated heterocyclic group including bicyclic ring such as piperidine, pyrrolidine, etc.).

Please amend the paragraph on page 40, lines 1-14 as follows:

Examples of the "optionally substituted carboxy" for R^2, R^3 and R^4 include carboxy, esterified carboxyl group (e.g., ester group where the carbonyloxy group is combined with C_{1-8} alkyl group such as methyl, ethyl, propyl, isopropyl, butyl, etc. which may be substituted at a suitable position with halogen, nitro, cyano, alkoxy, amino, substituted amino, etc., a C_{2-7} alkenyl group such as vinyl, allyl, etc., a C_{3-7} cycloalkyl group, a C_{3-7} alkylcycloalkyl group, a C_{5-7} cycloalkenyl group, a C_{5-7} alkylcycloalkyl group, an aromatic group (e.g., phenyl group, pyridyl group, etc.), benzyl group, or an alkylaromatic group (e.g. ~~benzyl group, methlypyridyl~~methylpyridyl group, etc.)) or amidated carboxyl group (e.g., amide group which may be substituted with C_{1-6} alkyl group such as methyl, ethyl, propyl, isopropyl, butyl, etc).

Please amend the paragraph on page 43, line 22 to page 44, line 10 as follows:

In the formula (I), Ar is an optionally substituted aryl or an optionally substituted heteroaryl. Examples of the "aryl" in the "optionally substituted aryl" for Ar include a C_{6-10} ~~Aryl~~aryl such as phenyl, naphthyl. The "heteroaryl" in the "optionally substituted heteroaryl" for Ar include, for example, a 5- or 6-membered nitrogen-containing aromatic heterocyclic ring which may have one or two further heteroatoms selected from oxygen, sulfur and nitrogen, such as furan, thiophene, pyrrole, imidazole, pyrazole, thiazole, oxazole, isothiazole, isoxazole, thiadiazole, oxadiazole, triazole, pyridine, pyrazine, pyrimidine, pyridazine, triazine.

Please amend the paragraph on page 99, lines 10-15 as follows:

When Z^1 is –SO- or –SO2- in compound (Ir) or a salt thereof, which is encompassed within (I) in the invention, can be ~~preapared~~ prepared by oxidation of compound (Ir) or a salt thereof. In this oxidation, 1 to 10 moles, preferably 1 to 5 moles of oxidation agent are employed per 1 mole of compound (Ir) or a salt thereof.

Please amend the paragraph on page 126, lines 14-17 as follows:

Compound (LXXXXI) or a salt thereof can be prepared by condensation of compound (LXXXX) or a salt thereof with trialkylorthoformate and amination of the alkoxymethylene compound or the salt ~~therof~~ thereof with $R^{1b}NH_2$.

Please amend the paragraph on page 138, line 20 to page 139, line 17 as follows:

Preferred examples of the solubilizing agent include polyethylene glycol, propylene glycol, benzyl benzoate, ethanol, ~~trisamiomethane~~trisaminomethane, cholesterol, triethanolamine, sodium carbonate, sodium citrate, and the like. Preferred examples of the

suspending agent include surface active agents such as stearyltriethanolamine, sodium lauryl sulfate, laurylaminopropionic acid, lecithin, benzalkonium chloride, benzethonium chloride, glycerin monostearate, and the like; hydrophilic, high molecular substances such as polyvinyl alcohol, polyvinyl pyrrolidone, sodium carboxymethyl cellulose, methyl cellulose, hydroxymethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, and the like; and so on. Preferred examples of the isotonicity agent include sodium chloride, glycerin, D-mannitol, and the like. Preferred examples of the buffering agent include buffer solutions of a phosphate, an acetate, a carbonate, a citrate, or the like. Preferable examples of the analgesic include benzyl alcohol and the like. Preferred examples of the preservative include paraoxybenzoic acid esters, chlorobutanol, benzyl alcohol, phenethyl alcohol, dehydroacetic acid, sorbic acid, and the like. Preferred examples of the antioxidant include sulfites, ascorbic acid, and the like.

Please amend the paragraph on page 143, line 14 to page 144, line 8 as follows:

To a solution containing 0.60 g (2.57 mmol) of 3-bromo-1-methyl-5-nitropyridin-2(*1H*)-one in 120 ml of toluene under a nitrogen atmosphere was added 0.64 ml (5.15 mmol) of 2,4-dimethylaniline, 1.61 g (2.57 mmol) of rac-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (racemic BINAP), 0.37 g (3.85 ~~mol~~mmol) of sodium t-butoxide and 1.20 g (1.31 mmol) of tris(dibenzylideneacetone)dipalladium (0). The reaction was heated to 95°C overnight. The reaction was cooled to room temperature, diluted with ethyl acetate and washed with saturated sodium bicarbonate. The organic phase was dried over magnesium sulfate. Filtration, removal of solvent and purification of the residue via biotage eluting with 60% ethyl acetate/hexanes gave the desired product with some starting aniline. The material was triturated with hexanes and the solids filtered and dried to afford 0.154 g (21.9%) of product.

Please amend the paragraph on page 147, lines 8-18 as follows:

4-Methoxy-6-methyl-N^2,N^2-dipropylpyrimidin-2,5-diamine (0.022 g, 0.092 mmol) was charged with 2,4,~~6-trimethyl-bromobenzene~~ 6-trimethylbromobenzene (16.7 μL, 0.11 mmol), *rac*-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) (0.012 g, 0.018 mmol), sodium *t*-butoxide (0.012 g, 0.13 mmol) and tris(dibenzylideneacetone) dipalladium (0) ($Pd_2(dba)_3$) (0.017 g, 0.018 mmol). The reagents were diluted in 1 mL of toluene and heated at 115 °C for 1.5 h. The solution was cooled and flash chromatographed (5% ethyl acetate/hexanes) to give 0.019g (58%) of the title compound as an oil.

Please amend the paragraph on page 150, lines 8-9 as follows:

6-(*N"*-~~Benzylidene-hydrazino~~Benzylidenehydrazino)-3-methyl-*1H*-pyrimidine-2,4-dione

Please amend the paragraph on page 150, lines 16-18 as follows:

^{1}H NMR ($CDCl_3$) δ: 3.10 (s, 3H), 4.95 (s, 1H), 7.40 – 7.42 (m, 3H), 7.88 (d, J = 6.4 ~~HZ~~Hz, 2H), 7.99 (s, 1H), 10.95 (bs, 2H).

Please amend the paragraph on page 152, lines 22-25 as follows:

^{1}H NMR ($CDCl_3$) δ: 0.89 (t, J = 7.2 Hz, 6H), 1.59 – 1.65 (m, 4H), 1.99 (s, 3H), 2.38 (s, 3H), 3.08- 3.23 (m, 4H), 3.43 (s, 3H), 5.12 (d, J= 14.4 Hz, 1H), 5.26 (d, J = 14.4 Hz, 1H), 7.03 – 7.20 (m, 5H), 7.21 – 7.24 (m, 3H).

Please amend the paragraph on page 164, lines 15-16 as follows:

2-Dipropylamino-3-methyl-4-oxo-3,4-~~dihydro-quinazolin~~dihydroquinazolin-5-yl-trifluoromethanesulfonate

Please amend the paragraph on page 165, line 13 to page 166, line 1 as follows:

To a mixture of 2-dipropylamino-3-methyl-4-oxo-3,4- ~~dihydro-quinazolin~~dihydroquinazolin-5-yl-trifluoromethanesulfonate (87 mg, 0.21 mmol), 2,4-dimethylphenylboroic acid (64 mg, 0.427 mmol) and potassium carbonate (59 mg, 0.43 mmol) and toluene (2 ml) was added of tetrakis(triphenylphosphine)palladium(0) (47 mg, 0.0405 mmol). The mixture was stirred at 90 °C for 18 h and diluted with water. The aqueous solution was extracted with ethyl acetate. The extract was washed with saturated sodium bicarbonate solution in water, 10% citric acid solution in water and brine, dried over magnesium sulfate, and concentrated under vacuum. The residue was purified by column chromatography eluting with 5% ethyl acetate /n-hexane to afford 55 mg (71 %) the title compound.

Please amend the paragraph on page 167, lines 23-24 as follows:

[1-(2-Ethylbutyl)-3-methyl-2,4-dioxo-1,2,3,4-~~tetrahydro-quinazolin~~tetrahydroquinazolin-5-yl]trifluoromethanesulfonate

Please amend the paragraph on page 168, line 19 to page 169, line 7 as follows:

To a mixture of [1-(2-ethylbutyl)-3-methyl-2,4-dioxo-1,2,3,4-~~tetrahydro-quinazolin~~tetrahydroquinazolin-5-yl]trifluoromethanesulfonate (29 mg, 0.071 mmol), 2,4-dimethylphenylboroic acid (21 mg, 0.14 mmol) and potassium carbonate (20 mg, 0.14 mmol) and toluene (2 ml) was added of tetrakis(triphenylphosphine)palladium(0) (41 mg, 0.036 mmol). The mixture was stirred at 90 °C for 18 h and diluted with water. The aqueous solution was extracted with ethyl acetate. The extract was washed with saturated sodium bicarbonate solution in water, 10% citric acid solution in water and brine, dried over magnesium sulfate, and concentrated under vacuum. The residue was purified by column chromatography eluting with 5% ethyl acetate/n-hexane to afford 11 mg (41 %) the title

compound.

Please amend the paragraph on page 169, line 20 to page 170, line 17 as follows:

A solution of (3-~~methyl-pyridin~~methylpyridin-2-yl)amine (10 g, 90 mmol) in 50 ml of concentrated sulfuric acid was cooled to 5°C in ice-salt bath. A mixture of 7 ml each of concentrated sulfuric acid and concentrated nitric acid was added slowly with stirring while maintaining the reaction temperature below 10 °C. This mixture was then allowed to warm to 30°C overnight. The solution was stirred rapidly while 7 ml of concentrated nitric acid was added at such a rate as to keep the temperature below 40°C. Approximately 10 ml of the solution was then poured into 20 ml of water and heated to 100°C; large quantities of gas were evolved. When gas evolution ceased, the remainder of the nitrating mixture was added in 10 ml portions with heating. When the last of the nitrating mixture had been added, the solution was cooled rapidly by placing the flask in an ice bath and by adding ice directly to the solution. The light brown precipitate was filtered and dried to afford 5.0 g (35%) of the title compound.

Please amend the paragraph on page 171, lines 12-19 as follows:

To a solution containing 0.2 g (0.73 mmol) of 1-(2,4- ~~dimethyl-benzyl~~dimethylbenzyl)-3-methyl-5-nitropyridin-2(1H)-one in 50 ml of methanol was added 0.017 g (0.073 mmol) of platinum (IV) oxide (Adam's catalyst). The flask was fitted with a balloon of hydrogen and allowed to stir for 1 h. The reaction was filtered through GF/F paper and the filtrate concentrated under reduced pressure to afford 0.11 g (62%) of product.

Please amend the paragraph on page 171, line 24 to page 172, line 9 as follows:

To a solution containing 0.04 g (0.165 mmol) of 5-amino-1-(2,4-~~dimethyl-benzyl~~dimethylbenzyl)-3-methylpyridin-2(1H)-one in 20 ml of methanol was added 0.1 ml

(1.6 mol) of propionaldehyde followed by 0.026 g (0.41 mmol) of sodium cyanoborohydride under a nitrogen atmosphere. The reaction was allowed to stir at 25°C overnight. The reaction was diluted with dichloromethane and washed with saturated sodium bicarbonate. The organic phase was dried over magnesium sulfate. Filtration, removal of solvent and purification of the residue via Biotage eluting with 20% ethyl acetate/ hexanes gave 0.025 g (46%) of product.

Please amend the paragraph on page 176, lines 4-14 as follows:

To a solution containing 0.2 g (0.74 mmol) of 5-(2,4-dimethylphenyl)-3-methyl-2-propylaminopyrimidin-4(*3H*)-one in 5 ml of tetrahydrofuran under a nitrogen atmosphere was added 0.12 g (2.2 mmol) of potassium hydroxide followed by 0.38 g (2.2 mmol) of 1-~~iodo-propane~~iodopropane. The reaction was allowed to stir at room temperature for 12h, diluted with ethyl acetate and washed with saturated sodium bicarbonate. The organic phase was dried over magnesium sulfate. Filtration, removal of solvent and purification of the residue via Biotage chromatography eluting with 30 % ethyl acetate /dichloromethane gave 0.15 g (65 %) of product.

Please amend the paragraph on page 178, line 14 as follows:

2-(2,4-Dimethylphenyl)~~-6-nitro-*N*-methylbenzamide~~-*N*-methyl-6-nitrobenzamide

Please amend the paragraph on page 179, line 15 to page 180, line 3 as follows:

A solution of sodium hydroxide (0.035g , 0.88 mmol) in water (2 ml) was added to a solution containing 0.095 g (0.33 mmol) of 2-(2,4-dimethylphenyl)~~-6-nitro-*N*-methylbenzamide~~-*N*-methyl-6-nitrobenzamide in methanol (1.5 ml). Zinc powder (0.03 g, 0.44mmol) was then added to the mixture, which was heated under reflux for 24 h. After cooling, the zinc residue was separated by filtration and the methanol was partially

evaporated. The residual solution was then adjusted to pH 7 with aqueous hydrochloric acid. The mixture was diluted with ethyl acetate and washed with saturated sodium bicarbonate. The organic phase was dried over magnesium sulfate. Filtration, removal of solvent and purification of the residue via biotage eluting with 40 % ethyl acetate/ hexanes gave 0.01 g (22%) of product.

Please amend the paragraph on page 180, lines 12- 22 as follows:

To a solution containing 0.008 g (0.03 mmol) of 4-(2,4-dimethylphenyl)-2-methyl-1,2-dihydro-*3H*-indazol-3-one in 2 ml of N,N-dimethylformamide under a nitrogen atmosphere was added 0.001 g (0.038 mmol) of sodium hydride followed by 0.007 g (0.048 mmol) of 3-~~bromo-pentane~~bromopentane. The reaction was allowed to stir at room temperature for 48h, quenched with water and extracted with ethyl acetate. The organic phase was dried over magnesium sulfate. Filtration, removal of solvent and purification of the residue via biotage eluting with 25% ethyl acetate/ dichloromethane gave 0.003 g (30%) of compound.

Please amend the paragraph on page 181, line 7 as follows:

Diethyl [[(3-bromophenyl)amino]~~]~~methylene]malonate

Please amend the paragraph on page 181, lines 19-20 as follows:

Ethyl 5-bromo-4-oxo-1-(1-propylbutyl)-1,4-~~dihydroquinoline~~dihydroquinoline-3-carboxylate

Please amend the paragraph on page 182, lines 1-9 as follows:

Diethyl [[~~(~~3-bromophenyl~~])~~amino]methylene]malonate (18.0 g, 53 mmol) was stirred in 100 mL of polyphosphate ester (PPE). The solution was heated for 3 h at 100 °C. The solution was cooled to room temperature and water was carefully added to form a precipitant. The

solution was filtered and the solid was washed with water. The precipitant was dried to give 24 g of the crude mixture of isomers.

MS Calcd.: ~~296~~295, Found: 296 (M+H) and 298 (~~M+2~~M+3H).

Please amend the paragraph on page 183, line 3 as follows:

MS Calcd. for (B): ~~394~~393, Found: 394 (M+H) 396 (~~M+2~~M+3H).

Please amend the paragraph on page 183, lines 6-23 as follows:

Ethyl 5-bromo-4-oxo-1-(1-propylbutyl)-1,4-dihydroquinoline-3-carboxylate, 0.977 g (2.48 mmol) of the isomeric mixture, and 7-bromo-4-oxo-1-(1-~~propyl-butyl~~propylbutyl)-1,4-dihydro-quinoline-3-carboxylic acid ethyl ester was dissolved in 6 mL of 48% hydrobromic acid. The solution was heated at 90 °C for 36 h. The solution was cooled and neutralized with saturated sodium carbonate. The solution was extracted using ethyl acetate (3 times), dried over magnesium sulfate and concentrated to give 0.700g of a yellow solid. The crude acid was dissolved in dimethyl sulfoxide (10 mL) and potassium cyanide (2.48 g, 38 mmol) was added. The reaction was heated to 115 °C for 9 h. The solution was cooled and diluted with ethyl acetate. The mixture was washed with water and brine. The organic phase was dried over sodium sulfate and concentrated. Flash chromatography (75% ethyl acetate/hexanes) gave 0.203 g (25% yield) of the title compound as an off white solid.

MS Calcd.: ~~322~~321, Found: 322 (M+H) 324 (~~M+2~~M+3H).

Please amend the paragraph on page 184, lines 18-19 as follows:

3-Bromo-5-(2,4-dimethylphenyl)~~3-bromo~~-1-(1-propylbutyl)quinolin-4(1H)-one

Please amend the paragraph on page 184, line 21 to page 185, line 9 as follows:

5-(2,4-Dimethylphenyl)-1-(1-propylbutyl)quinolin-4(1*H*)-one, (0.21 g, 0.61 mmol), was

dissolved in N,N-dimethylformamide (10 mL). The solution was cooled to 0°C and ~~N-bromosuccinamide~~ N-bromosuccinimide (0.11g, 0.62 mmol) was added. After 10 minutes, the solution was diluted with water, extracted with ethyl acetate, dried (Na_2SO_4), and concentrated. Flash chromatography (20% ethyl acetate/hexanes) gave 0.136g (53% yield) of the ~~5-(2,4-dimethylphenyl)-3-bromo-1-(1-propylbutyl)quinolin-4(1H)-one~~ title compound as a white solid.

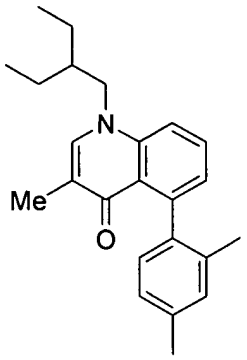
(MS Calcd.: ~~426~~425, Found 426 (M+H) 428 ~~(M+2)~~ (M+3H)).

Please amend the paragraph on page 185, line 15 to page 186, line 6 as follows:

~~The solid~~ 3-Bromo-5-(2,4-dimethylphenyl)-1-(1-propylbutyl)quinolin-4(1H)-one was then charged with methylboronic acid (0.19 g, 3.2 mmol), potassium carbonate (0.22 g, 1.6 mmol), tetrakis(triphenylphosphine)palladium(0) (0.18 g, 0.16 mmol) and diluted with dioxane (8 mL) under nitrogen gas. Water (29 μL, 1.6 mmol) was added last. The reaction was stirred at 90 °C overnight. The solution was cooled and concentrated. Flash chromatography (40% ethyl acetate/hexanes) gave 0.049 g (43% yield) of the title compound as a white solid.

^{1}H NMR ($CDCl_3$) δ: 0.85 – 0.97 (m, 6H), 1.20 – 1.36 (m, 4H), 1.81 – 1.90 (m, 4H), 1.96 (s, 3H), 2.02 (s, 3H), 2.36 (s, 3H), 4.65 – 4.70 (m, 1H), 6.96 – 7.04 (m, 4H), 7.47 (s, 1H), 7.52 – 7.59 (m, 2H).

Please amend the table on page 186 as follows:

Example	Structure	Name	Physical Data
25		5-(2,4-~~Dimethyl-phenyl~~Dimethylphenyl)-1-(2-ethylbutyl)-3-methyl-quinolin-4(*1H*)-one	^{1}H NMR ($CDCl_3$) δ: 0.94 - 1.00 (m, 6H), 1.37 - 1.45 (m, 4H), 1.96 (s, 3H), 1.95 - 2.00 (m, 1H), 2.00 (s, 3H), 2.37 (s, 3H), 3.91 - 4.01 (m, 2H), 6.96 - 7.04 (m, 4H), 7.38 - 7.40 (m, 2H), 7.55 - 7.60 (m, 1H). MS Calcd.: 347, Found: 348.

Please amend the paragraph on page 187, lines 3-13 as follows:

Dipropylamine (7.4 mL, 54 mmol) and 6-bromopyridine-2-carbaldehyde (5.0 g, 27 mmol) were dissolved in 1,2-dichloroethane (50 mL). 2 drops of glacial acetic acid was added followed by sodium triacetoxyborohydride (11.4g, 54 mmol). The reaction was stirred at 50 °C for 1 h. The reaction was cooled and quenched with water. The solution was diluted with saturated sodium bicarbonate and extracted with ethyl acetate (3 times). The organic layers were dried over magnesium sulfate, filtered and concentrated. Flash chromatography gave 5.34g (73% yield) of product.

MS Calcd.: ~~271~~270, Found: 271 (M+H) 273 (~~M+2~~M+3H).

Please amend the paragraph on page 189, lines 13-17 as follows:

^{1}H NMR ($CDCl_3$) δ: 0.88 (t, J = 7.2 Hz, 6H), 1.37 (t, J = 7.2 Hz, 3H), 1.35 – 1.47 (m, 4H), 1.97 (s, 6H), 2.30 (s, 3H), 2.89 (t, J= 6.0 Hz, 4H), 4.30 (q, J = 7.2, 14.4 Hz, 2H), 6.68 (d, J = 5.6 Hz, 1H), 6.85 (s, 2H), 7.39 – 7.43 (m, 1H), 8.26 (s, 1H), 8.34 (d, J = 7.2 Hz, 1H).

Please amend the paragraph on page 190, lines 2-12 as follows:

Ethyl 1-(dipropylamino)-6-mesityl-4-oxo-*4H*-quinolizine-3-carboxylate, (0.020 g,

0.046 mmol), in tetrahydrofuran (1 mL) was cooled to –40 °C. Diisobutylaluminum hydride (1.5M, 92 mL, 0.14 mmol) was added rapidly and the solution was warmed to room temperature. The reaction was quenched with methanol and stirred with saturated Rochelle's salt for 1 h. The solution was extracted with ethyl acetate, dried over sodium sulfate, filtered and concentrated. Flash chromatography (25% ethyl acetate/hexanes) gave 0.0107 g (59% yield) of the title compound as a yellow solid.

Please amend the paragraph on page 194, lines 2-11 as follows:

1-(Dipropylamino)-3-(hydroxymethyl)-6-mesityl-*4H*-quinolizin-4-one (0.60 g, 1.53 mmol) was dissolved in dichloromethane (20 mL) and acetonitrile (4 mL). 0.5g of crushed sieves (4 angstroms) was added followed by *N*-methylmorpholine *N*-oxide (NMO) (0.27 g, 2.3 mmol). Tetrapropylammonium perruthenate (TPAP) (0.081 g, 0.23 mmol) was added last. The reaction stirred for 0.5 h. The solution was filtered and concentrated. Flash chromatography (20% ethyl acetate/hexanes) gave 0.436 g (73% yield) of the title compound as a red solid.

Please amend the paragraph on page 197, line 20 as follows:

MS Calcd.: ~~276~~275, Found: 276 (M+H) 278 (~~M+2~~M+3H).

Please amend the paragraph on page 200, lines 12-16 as follows:

^{1}H NMR ($CDCl_3$) δ: 0.84 (t, J = 7.2 Hz, 6H), 1.31 (t, J = 7.2 Hz, 3H), 1.47 – 1.52 (m, 4H), 1.95 (s, 6H), 2.30 (s, 3H), 2.41 (t, J = 7.2 H, 4H), 3.68 (s, 2H), 4.29 (q, J = 7.2, 14.0 Hz, 2H), 6.73 (d, J = 6.0 Hz, 1H), 6.85 (s, 2H), 7.47 (t, J = 7.2 Hz, 1H), 8.09 (d, J = 9.2 Hz, 1H), 8.17 (s, 1H).

Please amend the paragraph on page 204, line 12 as follows:

MS Calcd.: ~~244~~243, Found: 244 (M+H) 246 (~~M+H~~M+3H).

Please amend the paragraph on page 204, line 15 to page 205, line 1 as follows:

1-(6-Bromopyridin-2-yl)pentan-2-ol (3.23 g, 13.2 mmol) was dissolved in 30 mL of 1,2-dimethoxyethane. Tetrakis(triphenylphosphine)palladium(0) (0.76g, 0.66 mmol) was added and the solution was heated to 50 °C for 15 min. After cooling the solution, 2,4,6-trimethylbenzeneboronic acid (2.60 g, 15.9 mmol) in 15 mL ~~1,2-dimethoxyethane~~ 1,2-dimethoxyethane was added to parent solution. Potassium *t*-butoxide (2.96g, 26.5 mmol) in 15 mL *t*-butanol was added last. The reaction was heated at 90 °C for 0.5 h. After cooling, the solution was filtered and concentrated. Flash chromatography (20% ethyl acetate/hexanes) gave the title compound (2.91 g, 77% yield).

Please amend the paragraph on page 209, line 8 as follows:

MS Calcd.: ~~188~~187, Found: 188 (M+H) 190 (~~M+2~~M+3H).

Please amend the paragraph on page 209, lines 11-22 as follows:

(6-Bromopyridin-2-yl)-methanol (4.23 g, 22.5 mmol) was dissolved in 1,2-dimethoxyethane. Tetrakis(triphenylphosphine)palladium(0) (1.30 g, 1.12 mmol) was added and the reaction stirred for 15 minutes at 50 °C. Upon cooling, 2,4,6-trimethylbenzeneboronic acid (3.69g, 22.5 mmol) in 20 mL ~~1,2-dimethoxyethane~~ 1,2-dimethoxyethane was added to the reaction followed by potassium t-butoxide (5.05g, 50.0 mmol) in 20 mL of *t*-butanol. The reaction was heated at 90 °C for 0.5 hr. The solution was cooled and filtered through paper. Flash chromatography (30% ethyl acetate/hexanes) gave the desired product as a white solid (3.50 g, 68% yield).

Please amend the paragraph on page 210, lines 16-17 as follows:

Diethyl [2-(6-mesitylpyridin-2-yl)-2-~~propoxy-ethylidene~~propoxyethylidene]-malonate

Please amend the paragraph on page 211, lines 7-14 as follows:

Diethyl 2-[2-propoxy-2-(6~~-mesityl-pyridin~~mesitylpyridin-2-yl)-ethylidene]~~-malonate~~ malonate (0.189 g, 0.43 mmol) was dissolved in 4 mL of Dowtherm A (phenyl ether: biphenyl 2:1 ratio). The solution was placed in a pre-heated oil bath set at 220°C. The reaction stirred at this temperature for 15 minutes. The solution was cooled and flash chromatographed (20-50% ethyl acetate/hexanes) to give 0.012g (7% yield) of the title compound.

Please amend the paragraph on page 215, lines 15-16 as follows:

^{1}H NMR ($CDCl_3$)δ: 2.10 (6H, s), 2.29 (3H, s), 2.85 (6H, s), 3.47 (3H, s), 3.72 (3H, s), 6.42 (1H, s), 6.90 ($2H_2$ s).

Please amend the paragraph on page 225, lines 14-15 as follows:

2-(Dipropionylamino)-5-mesityl-3,7-dimethyl~~-5-phenyl~~-3,7-dihydro-4*H*-pyrrolo[2,3-*d*]pyrimidin-4-one

Please amend the paragraph on page 242, lines 4-5 as follows:

(i) Ethyl ~~3-cyano-1-(2,4-dimethylphenyl)-1*H*-pyrrole-2-carboxylate~~3-cyano-1-(2,4-dimethylphenyl)-1*H*-pyrrole-2-carboxylate

Please amend the paragraph on page 254, line 3-9 as follows:

A mixture of diethyl ~~1-mesityl-1*H*-pyrrole-2,3-dicarboxylate~~1-mesityl-1*H*-pyrrole-2,3-dicarboxylate (3.4 g, 10.3 mmol), hydrazine monohydrate (2.0 ml, 41.3 mmol) and ethanol (20 ml) was heated under reflux for 48 hours. The mixture was acidified by addition of 5*N* hydrochloric acid and stirred at 80 °C for 20 min. After cooling, the crystals were collected by filtration to give 2.60 g (94%) of the title compound.

Please amend the paragraph on page 271, lines 5-6 as follows:

Methyl ~~1-benzyl-5-chloro-4-oxo-1,4-dihydrocinnoline-3-carboxylate~~1-benzyl-5-chloro-4-oxo-1,4-dihydrocinnoline-3-carboxylate

Please amend the paragraph on page 292, line 24 as follows:

MS Calcd.: 351; Found: 352 (M+H).

Please amend the paragraph on page 306, line 25 as follows:

MS Calcd.: ~~339~~338, Found: 339, 341 (~~M, M+2~~M+H, M+3H).

Please amend the paragraph on page 309, line 22 as follows:

MS Calcd.: ~~358~~357, Found: 358, 360 (~~M, M+2~~M+H, M+3H).

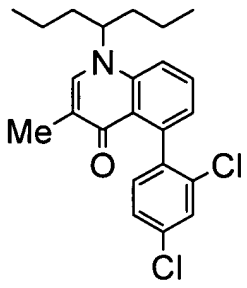
Please amend the paragraph on page 310, lines 10-13 as follows:

^{1}H NMR ($CDCl_3$) δ: 5.27 (s, 2H), 6.31 (d, J = 8.0 Hz, 1H), 7.12 (d, J = 8.0 Hz, 2H), 7.21-7.23 (m, 2H), 7.31-7.37 (m, 3H), 7.52-7.57 (m, 2H). MS Calcd.: ~~314~~313, Found: 314, 316 (~~M, M+2~~M+H, M+3H).

Please amend the paragraph on page 312, line 1 as follows:

MS Calcd.: ~~432~~431, Found: 432, 434 (~~M, M+2~~M+H, M+3H).

Please amend the table on page 314 as follows:

Example	Structure	Name	Physical Data
156		5-(2,4-dichlorophenyl)-3-methyl-1-(1-propylbutyl)quinolin-4(1H)-one	^{1}H NMR (acetone-*d6*) δ: 0.90 - 0.95 (m, 6H), 1.26 - 1.36 (m, 4H), 1.92 (s, 3H), 1.90 - 1.98 (m, 4H), 4.97 - 5.03 (m, 1H), 6.99 (d, J = 7.2 Hz, 1H), 7.21 (d, J = 8.4 Hz, 1H), 7.35 (dd, J = 2.0, 8.0 Hz, 1H), 7.45 (d, J = 1.6 Hz, 1H), 7.69 - 7.74 (m, 1H), 7.94 (s, 1H), 8.04 (d, J = 8.8 Hz, 1H). MS Calcd.: ~~402~~401, Found: 402, 404 (~~M, M+2~~M+H, M+3H).

Please amend the paragraph on page 338, lines 8-17 as follows:

A mixture of ~~*N*,3-dimethyl-4-nitro-1-(2,4,6-trichlorophenyl)-1*H*-pyrazole-5-carboxamide~~*N*,3-dimethyl-4-nitro-1-(2,4,6-trichlorophenyl)-1*H*-pyrazole-5-carboxamide (42 mg, 0.116 mmol) and tin (II) chloride (110 mg, 0.578 mmol) was stirred at 80 ^{o}C for 3 h and diluted with saturated sodium bicarbonate. The aqueous solution was extracted with ethyl acetate. The extract was washed with brine, dried over magnesium sulfate and concentrated under vacuum. The residue was purified by silica gel chromatography eluting with 50% ethyl acetate/hexane to give the title compound (20 mg, 52%).

Please amend the paragraph on page 338, line 24 to page 339, line 5 as follows:

To a solution of ~~4-amino-*N*,3-dimethyl-1-(2,4,6-trichlorophenyl)-1*H*-pyrazole-5-carboxamide~~ 4-amino-*N*,3-dimethyl-1-(2,4,6-trichlorophenyl)-1*H*-pyrazole-5-carboxamide (20 mg, 0.0600 mmol)in tetrahydrofuran (1 ml) was added phosgene (20% solution in

tetrahydrofuran, 0.048 ml) and the mixture was stirred at room temperature for 2 h. The solvent was evaporated under vacuum to give the title compound, which was used for the next step without further purification.

Please amend the paragraph on page 339, lines 11-17 as follows:

A mixture of ~~3,6-dimethyl-1-(2,4,6-trichlorophenyl)-1*H*-pyrazolo[4,3-*d*]pyrimidine-5,7(4*H*,6*H*)-dione~~ 3,6-dimethyl-1-(2,4,6-trichlorophenyl)-1*H*-pyrazolo[4,3-*d*]pyrimidine-5,7(4*H*,6*H*)-dione (20 mg, 0.0556 mmol), phosphorus oxychloride (0.52 ml) and *N,N*-diisopropylethylamine (0.21 ml) was stirred at 100 ^{o}C for 60 h. The solvent was evaporated under vacuum to give the title compound, which was used for the next step without further purification.

Please amend the paragraph on page 339, line 24 to page 340, line 9 as follows:

A mixture of ~~5-Chloro-3,6-dimethyl-1-(2,4,6-trichlorophenyl)-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one~~5-Chloro-3,6-dimethyl-1-(2,4,6-trichlorophenyl)-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one (20 mg, 0.0529 mmol) and dipropylamine (54 mg, 0.529 mmol) in *N,N*-dimethylformamide (1 ml) was stirred at 100 ^{o}C for 5 h and diluted with water. The aqueous solution was extracted with ethyl acetate. The extract was washed with brine, dried over magnesium sulfate and concentrated under vacuum. The residue was purified by silica gel chromatography eluting with 10% ethyl acetate / hexane to give the compound (A) (2.5 mg, 11%) and the compound (B) (8.1 mg, 40%).